PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2005/000623	18.02.2005	19.02.2004

International Patent Classification (IPC) or both national classification and IPC
C12Q1/26

Applicant
F2G LTD

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Authorized Officer

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18,19,22-24(IA)

because:

☒ the said international application, or the said claims Nos. 18,19,22-24(IA) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-9,11-20,22-25(partly)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-25(partly)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9,11,12,14-20,22-25
	No:	Claims	13
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9,11-20,22-25
Industrial applicability (IA)	Yes:	Claims	1-9,11-17,20,22-25
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/GB2005/000623

Re Item I
Basis of the opinion

1. Sequence listing pages 1-87 filed with the letter of 25.04.2005 do not form part of the application (Rule 13ter.1(f) PCT).

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 18, 19, 22-24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

2. Claims relating to inventions in respect of which no International Search Report has been established need not to be the subject of International Preliminary Examination (Rule 66(1)(e) PCT). Accordingly, only those parts which are identified in the International Search Report as having been searched (claims 1-9,11-20,22-25 (partly)), are subject of this International Preliminary Examination Report.

Re Item IV
Lack of unity of invention

1. The International Searching Authority considered that 20 inventions are present in the international patent application contrary to the requirements of Rule 13.1 PCT and invited the Applicant to pay additional searching fees (PCT/ISA/206).

   Invention 1: claims 1-25 (partly)
   An isolated protein comprising the sequence as defined in SEQ ID NO:3, methods, uses, vectors, organisms, antibodies and methods of treatments relating to said protein.

Invention 2: claims 1-25 (partly)
An isolated protein comprising the sequence as defined in SEQ ID NO:8, methods, uses, vectors, organisms, antibodies and methods of treatments relating to said protein.

Inventions 3/4/5.../20: claims 1-25 (partly)
An isolated protein comprising the sequence as defined in SEQ ID NO:12/14/19/24/42/83/85/6/10/16/22/27/30/33/35/38/40, methods, uses, vectors, organisms, antibodies and methods of treatments relating to said protein.

The single general concept that may possibly link the subject-matter of inventions 1-20 appears to reside in the provision of sequences encoding a fungal NADH:flavin oxidoreductase.

Database entry uniprot:Q870W3 discloses the NADH:flavin oxidoreductase as specified in SEQ ID NO:19 of the present application. In the light of this document, it appears that the single general concept lacks novelty and thus does not represent a single general inventive concept as required by Rule 13.1 PCT. The sequences identified in inventions 1-20 appear moreover not to be structurally related but are merely linked by the functional feature of being a NADH:flavin oxidoreductase. This, however, cannot be regarded to represent a special technical feature that could link the subject-matter of inventions 1-20 under Rule 13.2 PCT (see PCT Guidelines, 10.55). Thus, each of the above inventions represents an alternative solution to the technical problem of providing a further sequence encoding a NADH:flavin oxidoreductase.
In summary, the present application lacks unity, contrary to the requirements of Rule 13 PCT.

As no further search fees were paid by the Applicant, the International Search Report was established for the first and fully searched invention encompassing claims 1-25(partly) as far as the said claims related to SEQ ID NO:3.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Basis for the assessment of novelty, inventive step and industrial applicability

1.1 Reference is made to the following document/s/:

D1: DATABASE UniProt [Online] 1 May 1999 (1999-05-01), "SPBC23G7.10c protein." XP002333610 retrieved from EBI accession no. UNIPROT:O94467 Database accession no. O94467

D2: DATABASE Geneseq [Online] 13 March 2001 (2001-03-13), "Aspergillus oryzae EST SEQ ID NO:4627." XP002333611 retrieved from EBI accession no. GSN:AAF12104 Database accession no. AAF12104

D3: WO 03/025218 A (K.U.LEUVEN RESEARCH & DEVELOPMENT; LEMAIRE, KATLEEN; DE ROP, LARISSA;) 27 March 2003 (2003-03-27)

2. Novelty

2.1 Document D1 discloses a protein which is 50.938% identical (ungapped) to SEQ ID NO:3. Thus, claim 13 lacks novelty over D1 (Art 33(2) PCT).

2.2 Document D2 discloses a polynucleotide which encodes a protein falling under the definition of claim 13. Thus, claim 13 lacks novelty over D2 (Art 33(2) PCT).

3. Inventive step

3.1 Document D3 appears to be the closest prior art for claim 1. D3 discloses the screening for an anti-fungal compound that acts on (D3, Abstract; claim 7; page 5, lines 1-26). Claim 1 differs from closest prior art document D3 in the target molecule that is specified.

A technical effect which goes beyond the technical effects associated with the target

molecule in D3 appears not to be associated with the said difference.
The technical problem may be formulated as the provision of an alternative target molecule for a screening method of anti-fungal agents.
The solution as defined in claim 1 appears not to involve an inventive step (Art 33(3) PCT) as the said problem appears not to have been solved. The present application merely discloses that the protein encoded by SEQ ID NO:3 is essential for Aspergillus fumigatus (see Examples 1 and 2). This, however, cannot be assumed to be the case for the protein fragments defined in claim 1(iii), (iv), (v) and (vi). It is thus pure speculation as to whether the fragments specified therein are essential for a fungus or not. Therefore, the objective technical problem defined for claim 1 has not been solved and no inventive step can be acknowledged for claim 1 (Art 33(3) PCT). For the same reasons, also claim 9, 22, 23 and 25 lack an inventive step (Art 33(3) PCT).

3.2 In the light of documents D1 and D2, showing that the protein/nucleic acids as defined in claim 1 lack novelty over the prior art showing that these sequences exist in fungi, no inventive step can be acknowledged for a method of using these sequences to detect a fungus (Art 33(3) PCT).

3.1 As detailed in items 2.1 and 2.2 above, the sequences defined in claim 13 lack novelty over the prior art (Art 33(2) PCT). Starting from a known protein/nucleic acid, it falls within the routine of the skilled person to prepare a vector, a recombinant cell, a transgenic organism, an antibody, or the protein/the encoding nucleic acid as such. Thus, no inventive step can be acknowledged for claims 14-20 (Art 33(3) PCT).

4. Industrial applicability

4.1 The subject-matter disclosed in the claims 1-9, 11-17, 20, 22-25 of the present application appears to be industrially applicable (Art 33(4) PCT).

4.2 For the assessment of the present claims 18,19 22-24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for

example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

1. The expression "herein incorporated by reference" or equivalents thereof (e.g. page 71, line 8) does not comply with the Guidelines, Section IV, II-4.17.

2. The vague and imprecise statement in the description of the present application (page 71, lines 9-21) implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity of the claims (Art. 6 PCT) when used to interpret them (Guidelines, Section IV, III-4.3a).

3. The present application does not meet the requirements of Art 5 and Rule 5 PCT as documents D1-D3, which represent relevant prior art, are not referred to therein.